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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/089,475 | 08/12/2002 | Joshua W Hamilton | DC-0190 | 1040 |

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| EXAMINER | |
|---|---|
| PAK, MICHAEL D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 09/09/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/089,475 | HAMILTON ET AL. | |
| | Examiner | Art Unit | |
| | Michael Pak | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. The amendment filed 9 June 2008 has been entered. Claims 9 is examined below. Claims 1-8 and 10-11 are cancelled.

2. Applicant's arguments filed 9 June 2008, have been fully considered but they are not found persuasive.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moyer et al., in view of Riordan et al. (WO 01/03722), Cormack et al. (cited previously), McCray et al. (US 6,855,549), Chou et al.(cited previously), Dalemans et al. (US 6,136,594) and Caplan et al. (US 2004/0266883).

Moyer et al. teaches a method of measuring the effect of butyrate on the expression of a CFTR-GFP as set forth on page F272, column 2, third paragraph. The method is set forth on page F274 Figure 3. The term “EGFP" reporter gene is not defined in the specification and the claim limitation is met by the GFP taught by Moyer

et al. Moyer et al. teaches that butyrate partially restores cAMP-ativated Cl- secretion in CF epithelial cells by stimulating ΔF508 cystic fibrosis transmembrane conductance regulator (ΔF508-CFTR) gene expression and increasing the amount of ΔF508-CFTR in the plasma membrane (abstract).

Moyer et al. does not teach the mutant human CFTR protein having a deletion of the phenylalanine at amino acid position 508 (ΔF508). Moyer et al. does not teach the method of using proximal human CFTR promoter region. Moyer et al. does not teach the specific species of EGFP reporter gene. Moyer et al. does not teach the anthracyline agent in the method.

Riordan et al. teaches a method of increasing the amount of CFTR on cell surface of a cell by contacting with an agent (page 3, lines 25-31; page 4, lines 1-10; page 26, lines 11-19). Riordan et al. teaches a method using the cells expressing the ΔF508-CFTR by transfection of vector comprising the nucleic acid encoding ΔF508 (pages 15-22; page 26, line 18; pages 36-39).

Cormack et al. teaches the cloning of GFP mutants which fluoresce more intensely than wild type GFP (page 35, Figure2).

McCray et al. teaches the cumulative to Cormack et al. of a EGFP reporter construct with the CFTR (columns 1, 34 and 50).

Chou et al. teaches the transcription regulatory elements of the CFTR gene and that one was a proximal positive element delimited by the 5' deletion constructs -226 base pairs upstream of the transcription start site (page 24473, figure 2).

Dalemans et al. teaches a vector for expression in cell comprising the human CFTR gene which is under the control of the endogenous human CFTR promoter (abstract; column 2, lines 15-17 and lines 60-62). Dalemans et al. teach that ΔF508 is a mutant allele which is expressed at low level and associated with disease of CF (column 4).

Moyer et al. teach a method of using using the releasing agent activators to induce ΔF508 CFTR including curcumin, butyrate and anthracylcines such as doxorubicin or adriamycin (paragraphs 94, 197, 199 and claims 36 and 43).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Moyer et al. to substitute ΔF508 cDNA taught by Riordan et al. into the vector for transfection into a cell. One of ordinary skill would have been motivated by the teachings of Moyer et al. and Riordan et al. because of the importance of increasing the level of ΔF508 or CFTR in treatment of cystic fibrosis.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Moyer et al. and Riordan et al. to use the proximal human CFTR promoter region of Chou et al. One of ordinary skill in the art would have been motivated because Chou et al. teaches that the promoter of the CFTR can be used to obtain insights into the mechanisms governing the regulation of CFTR expression (page 24475, column 1, fourth paragraph). Furthermore, Dalemans et al. provides further motivation to use a vector to transfect and express in cells CFTR genes and to use the endogenous promoter.

If in arguendo, applicants argue that the term "EGFP" is not encompassed by the teaching of Moyer et al. GFP, then following analysis is made. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify method of Moyer et al. by using the modified GFP of Cormack et al. or EGFP of McCray et al. One of ordinary skill in the art would have been motivated because Cormack teaches that optimized GFP has a greatly increased fluorescence intensity, making the mutants useful for a number of applications (page 37, column 2, second paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Moyer et al., Riordan et al., Chou, Cormack et al., and McCRay et al. by using the anthracycline agent in the method of Caplan et al. One of ordinary skill in the art would have been motivated because Chou et al. teaches that the activating agents such as butyrate and anthracycline are well known in the art and maybe useful for the method (paragraphs 197 and 199)).

The products used in the methods are well known to one of skilled in the art and all the references are analogous references which provide additional motivation to combine the references.

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael Pak/
Primary Examiner, Art Unit 1646
September 1, 2008